ments of the left anterior descending coronary artery (LAD) included lumen area, intimal area, intimal index and maximal intimal thickness (MIT). Results revealed a significant progression of intimal thickening in all patients (MIT year 0 = 0.26 ± 0.23 mm vs. year 1 = 0.40 ± 0.28 mm, $p < 0.01$) and no evidence of compensatory dilation even in those patients with a change in MIT ≥ 0.15 (n = 20) and ≥ 0.3 mm (n = 6). There was a greater progression of disease in the proximal compared to the more distal LAD, but not when correcting for lumen size (i.e., intimal index). There was significantly more disease at branch sites compared to sites between branches for all measurements at baseline and at one year (year 1: MIT at branches = 0.55 ± 11 mm vs. MIT morphometry = 0.39 ± 0.11, $p < 0.01$), although the absolute progression of disease was similar at and between branch sites.

Conclusion: In the first year after heart transplantation there is significant progression of TCAD without evidence of compensatory vessel dilation, greater proximal coronary artery disease and more disease adjacent to branch vessels. Due to the heterogeneity of TCAD, quantitative morphometric analysis most accurately represents the severity of TCAD.

8:45

776-2 Simultaneous Intravascular Ultrasound and Doppler Wire Studies Demonstrate a Dissociation Between Coronary Flow and Area Responses Following Heart Transplant

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Paradoxical epicardial vasoconstriction in response to the endothelium-dependent vasodilator acetylcholine (Ach) is felt to indicate endothelial dysfunction. Such epicardial vasoconstriction has been shown early following orthotopic heart transplantation (OHT), but the extent to which such dysfunction extends to the microvasculature is not clear. *Methods:* Diameter and velocity responses were studied in 10 patients 2–7 weeks status post OHT, all with normal coronary angiograms, using a 3.5 F 30 mHz IVUS catheter positioned over a 0.014" Doppler wire in the LAD. Sequential intracoronary infusions of adenosine (Aden, 16 and 32 μg bolus), acetylcholine (Ach, 54 μg over 2 min) and nitroglycerin (NTG, 200 μg bolus) were given, with continuous IVUS imaging and Doppler velocity measurements. Maximal vessel cross-sectional area and coronary flow velocities were measured and expressed as % of baseline (BL). Flow was calculated as the product of vessel area and velocity. *Results:* Ach induced paradoxical vasoconstriction in 7 of 10 pts (84 ± 6% of BL); vasodilation occurred in 3 (105 ± 2%). Despite this constriction, coronary flow increased in all 10, to the same extent in dilators and constrictors (218 ± 17 vs 281 ± 47, $p = 0.12$). The endothelium-dependent resistance vessel dilator Aden increased area (107 ± 1%) and flow (298 ± 28%) in all pts. NTG, an endothelium-independent vasodilator, also increased vessel diameter (112 ± 4%) and flow (209 ± 14%). *Conclusions:* Despite epicardial vasoconstriction, Ach increases flow early after OHT, suggesting that microvascular responses to Ach were preserved. Responses to Aden and NTG were normal as well. These disparate responses between area and flow suggest that paradoxical epicardial vasoconstriction to Ach may not indicate microvascular endothelial dysfunction. Simultaneous IVUS and Doppler wire studies may provide more comprehensive and clinically useful assessment of coronary endothelial function.

9:00

776-3 Can Annual Surveillance Coronary Angiography After Heart Transplantation Be Substituted by Noninvasive Dobutamine Stress Echocardiography?

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Coronary angiography (ANGIO) is performed annually by most centers for diagnosis of allograft vasculopathy (CAV). In this study, the impact of routine ANGIO findings on patient (P) care late (≥ 12 months) after heart transplantation (HTX) was analyzed. ANGLO was compared to quantitative intravascular ultrasound (IVUS; modified Stanford grading, grades 1–6) and dobutamine stress echocardiography (DSE, 5–40 mcg/kg/min; assessment of wall motion abnormalities (WMA)). 165 ANGIOs (1–5/P) were performed in 62 P (51 ± 10 yrs) mean 59 ± 33 (12–144) months after HTX. A total of 89 IVUS studies were done in 48 P, 102 DSE studies were performed in 55 P.

Results: ANGIO evidence of CAV was seen in 18/62 P (29%) in 27/165 ANGIOs. Indication for revascularization was seen in 6 ANGIOs in 5/62 P (PTCA, n = 4; subsequent re-HTX, n = 1; primarily re-HTX, n = 1). 29/48 P (60%) had intimal hyperplasia indicating CAV (mean IVUS grade > 3.0; 45/89 studies). 18/44 P with normal ANGIO had IVUS evidence of CAV. DSE identified WMA in 50/102 studies in 27/55 P (49%, including all P with PTCA/re-HTX). Newly developed WMA in P studied serially were associated with angiographic and/or IVUS progression of CAV. Sensitivity (specificity) of DSE for detection of P with angiographic CAV was 88% (61%), for detection of IVUS evidence of CAV 82% (86%). In 28 P with normal DSE, neither myocardial infarction nor death were observed during a follow up period of 18 ± 6 (3–31) months.

Conclusions: ANGIO underestimates the incidence of CAV, compared to IVUS. DSE is a sensitive noninvasive method for screening of angiographic CAV and even early IVUS evidence of CAV. DSE identified all P with subsequent PTCA/re-HTX. Normal DSE findings predict a low probability of clinical events at follow-up. Thus, costly and invasive annual ANGIO is not necessary in every HTX-P. A normal DSE study may substitute routine ANGIO after HTX.

9:15

776-4 IGF-I Accelerates Transplant Arteriosclerosis *in Vivo*

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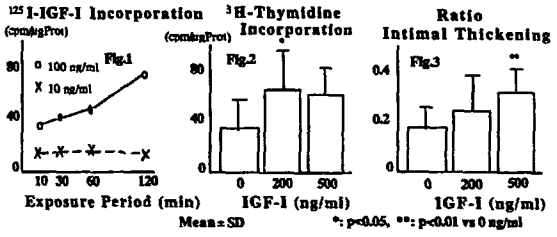
The development of transplant arteriosclerosis (TA) is a major limiting factor for long time survival of transplanted organs. The mechanisms remain unknown but undiagnosed rejections eliciting release of growth factors are thought to be involved in accelerating myointimal proliferation. We hypothesized that IGF-I may be a crucial growth factor in this process. Thus, we studied the effect of IGF-I on the acceleration of rat aortic TA following orthotopic allograft *in vivo*. We first evaluated the feasibility of IGF-I incorporation into the arterial wall after a short exposure period *ex vivo*. Abdominal rat aortas (AAo) of the donor strain, Brown Norway (BN, n = 3), were harvested and placed in DMEM at 37° C with 10 or 100 ng/ml of ^{125}I-IGF-I for up to 120 minutes. Fig. 1 demonstrates a time dependent incorporation of IGF-I at 100 ng/ml but not at 10 ng/ml. AAo from the donor rats (BN) were placed in 0, 200, or 500 ng/ml of IGF-I solution for 30 minutes and transplanted into histoincompatible recipient rats (Lewis). Tritiated thymidine incorporation of the vascular wall was determined at 7 days (n = 4). The degree of intimal thickening was examined at 14 days (n = 7) using computerized morphometry. The proliferation was expressed as the ratio of intimal area to total vascular area [I/(I + M)], (Figs. 2, 3).



Local exposure to IGF-I following donor harvesting but prior to transplantation, with no systemic administration of IGF-I, results in increased cell proliferation and accelerated TA *in vivo*, suggesting an important role for IGF-I in TA.

9:30

776-5 Cytomegalovirus Accelerates Allograft Arteriosclerosis in Cardiac Transplant Recipients

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The role of CMV infection in the pathogenesis of allograftarteriosclerosis (AA) is controversial. Previous studies have relied on angiography, but intravascular ultrasound (IVUS) is more sensitive in detecting early coronary pathology. To investigate the relationship between active CMV infection and AA, we examined serial CMV serologies in 76 cardiac transplant pts undergoing IVUS. Pts were classified as: new seroconversion or reactivation (S), convalescent (C), history of recipient CMV (S + C), or unexposed naive (N). The mean maximal intimal index (%) and intimal thickness (μm) of pts with evidence

	n	Days to Study	Intimal Index	Intimal Thickness
S	21	708 ± 80	13 ± 3	310 ± 60
C	32	866 ± 93	11 ± 2*	310 ± 40*
S + C	53	843 ± 74	12 ± 1*	310 ± 40*
N	23	768 ± 106	8 ± 4	18 ± 60

*$p \leq 0.05$ compared to N